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Fax Cover Sheet

Date: 16 Jan 2003

To: Paul Carango	**From:** Mary M. Schmidt
Application/Control Number: 09/435,249	**Art Unit:** 1635
Fax No.: 215-988-1809	**Phone No.:** (703) 308-4471
Voice No.:	**Return Fax No.:** (703) 746-5264
Re:	**CC:**

☐ **Urgent** ☐ **For Review** ☐ **For Comment** ☐ **For Reply** ☐ **Per Your Request**

Comments:
Attached is a copy of the response filed on Sept. 9, 2002 (7 pages).

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Comments:
Attached is the interview summary dated 1/15/03.

Number of pages __ including this page

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Patent Technology Center 1600

Facsimile Transmission

To:	**Name:**	Paul Corrango
	Company:	
	Fax Number:	215-988-1809
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From:	**Name:**	Melissa Schmidt
	Official Fax Number:	**(703) 872-9306**
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DOCKET NO.: TJU-2503 (SCH01.NP001)

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Ray S. Schneider

Serial No.: **09/435,249** Group Art Unit: **1635**

Filed: **November 5, 1999** Examiner: **M. Schmidt**

For: **Treatment Of Parkinson's Disease With Oligonucleotides**

I, Mark DeLuca, Registration No. 33,229, certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

On September 4, 2002

Mark DeLuca, Registration No: 33,229

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

AMENDMENT AND REQUEST FOR RECONSIDERATION

In response to the Office Action mailed June 5, 2002 in connection with the above-identified patent application, Applicant requests that the application be amended as follows.

In the Specification:

Please replace the paragraph beginning on page ~~8~~ 9, line ~~27~~ 7 with the following paragraph:

These sequences were obtained by searching Genbank for the appropriate gene name. These sequences were analyzed using an open reading frame finder program at the National Center for Biotechnology Information and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/gorf/orfig. The initiation of translation site was found and a 21 base antisense molecule complementary to the region spanning 8 bases 5' to 13 bases 3' (-8 to

+13) to the initiation triplet was selected. These 21 base oligonucleotides were analyzed for cross reactivity with other genes using the NCBI BLAST server and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/BLAST/.

In the Claims:

Please cancel claims 27 and 33, amend claims 23, 28 and 30, and add new claims 34-37 as follows:

23. (Amended) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of an antisense oligonucleotide effective to inhibit translation of glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

28. (Amended) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide effective to inhibit translation of glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

30. (Amended) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula, wherein said antisense oligonucleotide is directed to the initiation codon of glutamic acid decarboxylase mRNA, and said antisense oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.

34. (New) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of antisense oligonucleotides effective to inhibit translation of

glutamic acid decarboxylase GAD_{65} and GAD_{67} mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase.

35. (New) The method of claim 34 wherein said antisense oligonucleotides are directed to the initiation codon of an glutamic acid decarboxylase mRNA.

36. (New) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering antisense oligonucleotides effective to inhibit translation of glutamic acid decarboxylase GAD_{65}, and GAD_{67} mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula.

37. (New) The method of claim 28 wherein said antisense oligonucleotide are directed to the initiation codon of an glutamic acid decarboxylase mRNA.

REMARKS

Status of the claims

Claims 1-4, 9-12 and 23-33 are pending in the application.

Claims 1-4 and 9-12 have been allowed.

Claims 23-29 and 31-33 have been rejected.

Claim 30 has been objected to.

By way of this amendment, claims 27 and 33 have been canceled, claims 23, 25, 26, 28 and 30-32 have been amended, and new claims 34-37 have been added.

Upon entry of the amendment, claims 1-4, 9-12, 23-26, 28-32 and 33-37 will be pending.

Summary of the Amendment

The specification has been amended to delete URL designations. No new matter is added.

Claims 27 and 33 have been canceled in favor of new claims 34 and 36 respectively. New claims 34-37 refer to embodiments of the invention in which a combination of antisense compounds

directed to inhibit expression of both the GAD_{65}, and GAD_{67} isoforms are used. Support for new claims 34-37 is found throughout the specification and claims as originally filed. No new matter has been added.

Claims 23 and 28 have been amended to more clearly recite that the oligonucleotides used in the claimed methods are effective to inhibit expression of GAD_{65}, or GAD_{67}. As amended, the claims are limited to those embodiments in which the oligonucleotide is functional. Support for the amendment is found throughout the specification and claims as originally filed. No new matter has been added.

Claim 30 has been amended to incorporate all of the limitations of claim 29 from which it depended. Support for the amendments is found throughout the specification and claims as originally filed. No new matter has been added.

Preliminary Remarks

As a preliminary matter, Applicants acknowledge that that the subject matter in claims 1-4, 9-12 and 23-33 has been deemed free of the prior art, and that claims 1-4 and 9-12 are allowable. Applicants present this amendment to place the remaining claims in allowable form.

Specification

Objections were made to the specification for the inclusion of hyperlinked text on pages 8 and 9. The objected to text has been deleted and the objection is obviated.

Rejections under 35 USC §112

Claims 23-29 and 31-33 stand rejected under 35 U.S.C. § 112, first paragraph, because it is asserted that the specification fails to provide an enabling disclosure "for administration of any of (*sic*) antisense to GAD as instantly claimed." (Page 3 of Official Action). Applicants respectfully disagree.

The reason provided in support of the rejection is that the teachings in the specification do "not correlate to the design and use of any other individual antisense oligonucletide." (Page 3-4 of Official Action). It is asserted that the specification is not enabled for antisense to any GAD gene.

The claims have been amended to more specifically recite the scope of the claims in an effort to more clearly set forth the invention as enabled. Amended claims 23 and 28 recite that the

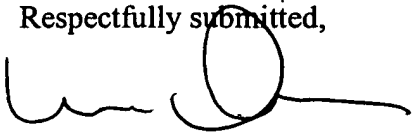
glutamic acid decarboxylase is GAD_{65} or GAD_{67} and that the antisense oligonucleotide inhibits expression of GAD_{65} or GAD_{67} mRNA. One skilled in the art would be able to practice the claimed invention without being required to perform undue experimentation.

Those skilled in the art could routinely produce, test and identify the various antisense oligonucleotides within the scope of the invention without undue experimentation. There is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation in order to make and use the claimed invention. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are in condition for allowance. An early notice of the same is earnestly solicited. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



Mark DeLuca
Registration No. **33,229**

Date: Sept 4 2002

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One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The following paragraph beginning on page 8, line 27 has been amended as follows:

These sequences were obtained by searching Genbank for the appropriate gene name. These sequences were analyzed using an open reading frame finder program at the National Center for Biotechnology Information [World Wide Web site (http://www.ncbi.nlm.nih.gov/cgi-bin/gorf/orfig)] and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/gorf/orfig. The initiation of translation site was found and a 21 base antisense molecule complementary to the region spanning 8 bases 5' to 13 bases 3' (-8 to +13) to the initiation triplet was selected. These 21 base oligonucleotides were analyzed for cross reactivity with other genes using the NCBI BLAST server [(http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/)] and is publicly available through the Internet at the world wide web at, for example, ncbi.nlm.nih.gov/cgi-bin/BLAST/.

In the Claims:

Claims 27 and 33 have been canceled. Claims 34-37 have been added and claims 23, 28 and 30 have been amended as follows:

23. (Amended) A method of treating Parkinson's disease in a mammal, comprising administering a therapeutically effective amount of an antisense oligonucleotide effective to inhibit translation of [directed to] glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula for the downregulation of glutamic acid decarboxylase wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

28. (Amended) A method of downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide effective to inhibit translation of [directed to]

glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula wherein said glutamic acid decarboxylase is GAD_{65}, or GAD_{67}.

30. (Amended) A [The] method of [claim 29] downregulating glutamic acid decarboxylase in a mammal *in vivo* comprising administering an antisense oligonucleotide directed to glutamic acid decarboxylase mRNA to the substantia nigra pars reticulata or internal globus pallidus via a cannula, wherein said antisense oligonucleotide is directed to the initiation codon of glutamic acid decarboxylase mRNA, and said antisense oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:5.